

Notice of Allowability

Application No.

10/765,227

Examiner

Susannah Lee

Applicant(s)

KUKI ET AL.

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to Applicant's Response to first Office Action June 28, 2005.
2. ☒ The allowed claim(s) is/are 1-12, 14 and 15.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 5/7/04, 6/11/04 and 11/2/04.
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413),
Paper No./Mail Date _____.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Claims 1 – 23 are pending in the instant application and were the subject of a first Office Action dated April 1, 2005. **Claims 13 and 15 – 23** were not examined in the first Office Action as drawn to a non-elected invention; however, upon allowance of the product claims, the restriction requirement was withdrawn and the claims rejoined. **Claim 13 and Claims 16 – 23** were subsequently cancelled by Examiner's Amendment authorized by applicant (note: **Claim 15** was not cancelled after rejoinder). **Claims 1 – 12, 14 and 15**, as amended, were found to be free of the art and allowable. No new matter was found. An Examiner's Amendment and Statement of Reasons for Allowance follow below.

Priority

This application claims benefit of U.S. Provisional Application No. 60/443,223, filed January 27, 2003, per the amended Application Data Sheet dated March 23, 2005.

Information Disclosure Statement

The Information Disclosure Statements filed on May 7, 2004, June 11, 2004, and November 2, 2004, are in compliance with 37 C.F.R. §1.97, and were considered by the examiner.

Response to Applicant's Response to First Office Action

Applicant's Response to the first Office Action, received June 28, 2005, is hereby acknowledged.

Claims 1 – 4 and 14 were rejected in the first Office Action pursuant to 35 U.S.C. §103(a) over **U.S. Patent No. 5,010,077 (Braestrup, et al.)** in view of the teaching in **Beng Ho, et al.**, "Inhibitors of Monoamine Oxidase: Influence of Methyl Substitution on the Inhibitory

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Activity of β -Carbolines,” J. Pharmaceutical Sciences, vol. 57, pages 269 - 274 (Feb. 1968). The examiner thanks applicant for the thorough analysis applying these two references to the pending claims, and determines that the applicant’s reasoning is persuasive, particularly in view of the absence of “blazemarks” or other indicators in U.S. Patent No. 5,010,077 directing the person of skill in the art toward substitution of the indolic nitrogen atom with a non-hydrogen group. Thus, the examiner’s rejections to **Claims 1 – 4 and 14** are overcome by applicant’s Response to the First Office Action, and the rejections brought under 35 U.S.C. §103(a) are expressly withdrawn as to **Claims 1 – 4 and 14**.

Claims 5 – 12 were objected to in the first Office as dependent upon rejected base claims. These objections are obviated by the withdrawal of the rejection to **Claims 1 – 4 and 14** described above. **The objections to Claims 5 – 12 are therefore expressly withdrawn by the examiner.**

New Matter Analysis

No new matter was included in the amendments to the claims (see examiner’s amendment below).

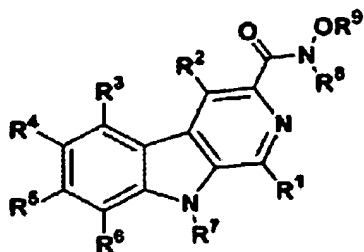
Withdrawal of Restriction Requirement

The examiner’s restriction requirement, written in the first Office Action (dated April 1, 2005) is hereby expressly withdrawn.

Scope of prior art searched

The search of the prior art was expanded beyond the scope of the art searched in the first Office Action (dated April 1, 2005), so as to include those β -carboline compounds of Formula

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(I), (II), substituted at the 3-position with an hydroxamic acid group $C(=O)NR^8OR^9$, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 and R^9 were as defined in **Claim 1**, as amended. The compounds thus defined were found to be free of the prior art of record.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Agreement for the following examiner's amendment was reached in a telephone interview with Jeffrey H. Tidwell, Esq., on September 19, 2005. Applicant authorized the following amendments to the Claims:

Delete Claim 13.

Delete Claims 16 – 23.

In **Claim 1**, page 49, lines 19-20, delete "and pharmaceutically acceptable salts and solvates thereof" and insert ---or a pharmaceutically acceptable salt or solvate thereof---.

In **Claim 3**, page 49, line 26, insert ---and--- after the terms "wherein said aryl, cycloaryl," and before the term "heterocycloalkyl".

In **Claim 3**, page 49, line 27, delete the term "and heteroaryl".

In **Claim 5**, page 50, line 5, delete "," [semicolon] after the term $-NH_2$ and insert ---,--- [comma].

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In **Claim 5**, page 50, line 6, delete “(5-chlorothien-2-yl)methyl,” after the terms R^7 is 4-fluorobenzyl.

In **Claim 12**, page 51, lines 15-16, delete “9-[(5-chlorothien-2-yl)methyl]-N-hydroxy-9H- β -carboline-3-carboxamide;”.

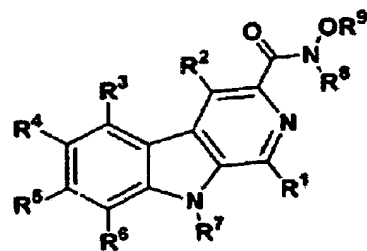
In **Claim 12**, page 51, line 24, insert ---and--- before the term 9-(4-fluorobenzyl).

In **Claim 12**, page 51, lines 24-25, delete “and pharmaceutically acceptable salts and solvates thereof” and insert ---or a pharmaceutically acceptable salt or solvate thereof---.

The cancellation of **Claims 13 and 16 – 23** was without prejudice for applicant to pursue in a future continuing or divisional application.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: The present invention

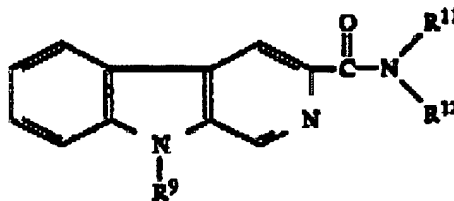


(I)

is directed to compounds and compositions of Formula (I)

wherein substituents $R^1 - R^9$ are as defined in **Claim 1**.

The closest prior art of record is U.S. Patent No. 5,010,077 (Braestrup, et al.) which



(col.

taught β -carboline derivatives having the structure

21, line 2), including a specific embodiment where R^{11} was H, R^{12} was $-OH$, and where R^9 was H, thereby yielding a compound with a melting point of $237.5^\circ - 239^\circ C$. U.S. Patent No.

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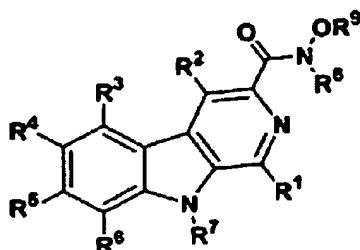
5,010,077, at col. 21, line 16 (Table III); see also *id.* at col. 35, lines 53 – 55 (claim 3). This particular species was the only one disclosed in this patent in which the substituent at the 3-position on the β -carboline ring was a hydroxamic acid group.

U.S. Patent No. 5,010,077 also claimed the “pharmaceutical compositions” of these compounds, which is relevant to **Claims 14 and 15** of the present invention. See U.S. Patent No. 5,010,077 at col. 36, lines 17 – 18 (Claim 5).

The compounds and compositions of the present invention are distinguished from the prior art by the presence of a “hydroxamic acid” group at the 3-position of a β -carboline ring *combined with* the limitation that the indolic nitrogen atom (i.e., at the 9-position of the β -carboline ring) be substituted with an alkyl, alkenyl or alkynyl group.

Note: Although **U.S. Patent No. 5,010,077** disclosed the range of values for substituent **R⁹** as “hydrogen, *C₁₋₈ alkyl*, *C₁₋₈ alkenyl*, *C₁₋₈-alkoxycarbonyl*, *C₁₋₈-alkenyloxycarbonyl*, or *C₁₋₈-alkenyloxy*,” [emphasis added] in the Abstract and Specification, this patent provided no specific embodiments of his invention where the substituent on the indolic nitrogen atom (i.e., **R⁹**) was “*C₁₋₈ alkyl*,” (or any substituent other than a hydrogen atom, except for a single species substituting an ethyl ester at this bonding site); nor did this patent provide any blazemarks or motivation for the skilled artisan to substitute an alkyl, alkenyl or alkynyl group at that particular bonding site where the substituent at the 3-position was a hydroxamic acid group. See, e.g., id. at col. 3, lines 6 and 50; col. 11 (“Table V”); Examples 1 – 75; and col. 20 (“Table III”); compare col. 21, line 50 (ethyl ester). In view of the state of the art for β -carboline derivatives at the time of this application, the compounds and compositions disclosed in **U.S. Patent No. 5,010,077**, which are the closest prior art, do not anticipate, or render obvious, the compounds

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and compositions of formula (I)

(I) of the present invention. For

the same reasons, the compositions of such compounds and a pharmaceutically acceptable carrier, diluent or vehicle (i.e., **Claims 14 and 15**) would likewise not be anticipated nor rendered obvious by the compositions disclosed in the closest prior art.

For all of the reasons above, **Claims 1 – 12, 14 and 15** (as amended) are neither anticipated nor rendered obvious over the prior art of record, and are therefore allowable.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should accompany the issue fee. Such submissions should be clearly labeled as “Comments on Statement of Reasons for Allowance.”

Conclusion

Claims 1 – 12, 14 and 15, as amended, are allowable.

Claim 13 and Claims 16 – 23 were cancelled by Examiner’s Amendment authorized by applicant.

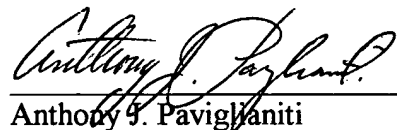
Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Anthony J. Paviglianiti** whose telephone number is (571) 272-3107. The examiner can normally be reached on Monday-Friday, 8:30 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Joseph K. McKane, can be reached at (571) 272-0699. **The fax phone number for**

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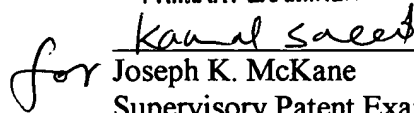
the organization where this application or proceeding is assigned is (571) 273-8300. Please note that this is a new central FAX number for all official correspondence.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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